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CLAIMS:

1. A system for use in producing a polyketide having substantially exclusively a desired starter unit by providing a PKS multienzyme which comprises a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for transfer to an adjacent one of said extension modules, and wherein at least one of the extension modules is not naturally associated with a loading module that effects decarboxylation; with the proviso that the target polyketide is not a 14-membered macrolide having a 13-methyl group due to incorporation of an (unsubstituted) acetate starter unit.

2. A system according to claim 1 wherein said adjacent extension module to which the acetate starter is transferred is not naturally associated with a loading module that effects decarboxylation.

3. A system according to claim 1 ~~or 2~~ wherein the decarboxylating functionality of the loading module is provided by a ketosynthase-type domain having a glutamine residue in the active site or other residue other than cysteine.

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a 4. A system according to claim 1 ~~or 2~~ wherein the decarboxylating functionality of the loading module is provided by a CLF-type domain.

a 5. A system according to ^{claim 1} ~~any of claims 1 to 4~~ wherein the loading module's loading functionality is provided by an acyltransferase-type domain having an arginine residue in the active site.

a 6. A system according to ^{claim 1} ~~any of claims 1-5~~ wherein the loading module includes an acyl carrier protein.

a 7. A system according to ^{claim 1} ~~any of claims 1-3, 5 or 6~~ wherein at least the Ksq domain of said loading module corresponds to the loading module of the PKS multienzyme of oleandomycin, spiramycin, niddamycin, methmycin or monensin.

8. A PKS multienzyme as expressible by the DNA of the system of any of claims ~~1~~ to 7 or a variant having the ability to synthesize a said polyketide compound.

a 9. Nucleic acid encoding the PKS multienzyme of claim ¹⁶ ~~8~~.

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10. A vector containing nucleic acid as defined in claim 9.

11. A transformant organism comprising a system according to ^{claim 1} ~~any of claims 1 to 7~~.

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12. A process for producing a polyketide which comprises culturing an organism according to claim 11 and recovering the polyketide.

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13. A system, multienzyme, nucleic acid, vector, organism or process according to any preceding claim wherein said polyketide is selected from

(a) 12- and 16-membered macrolides with acetate starter units

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(b) 12, 14 and 16-membered macrolides with propionate starter units

sub a2
(c) variants of rifamycin, avermectin, rapamycin, immunomycin and FK506 with acetate starter units or propionate starter units

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(d) a polyketide wherein the starter unit gave rise to a sidechain selected from allyl and hydroxymethyl.

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14. A variant of a parent polyketide which differs from the parent polyketide in the side chain provided by the starter unit.

- 5 15. A process for preparing a type II polyketide comprising culturing an organism containing a type II polyketide synthase ("PKS") wherein the wild type synthase includes a CLF domain which tends to effect decarboxylation to produce an undesired starter; wherein said organism contains a PKS which has been genetically engineered to
- 10 suppress the decarboxylating activity of said CLF domain.

add
a³

add
a³

add
a¹